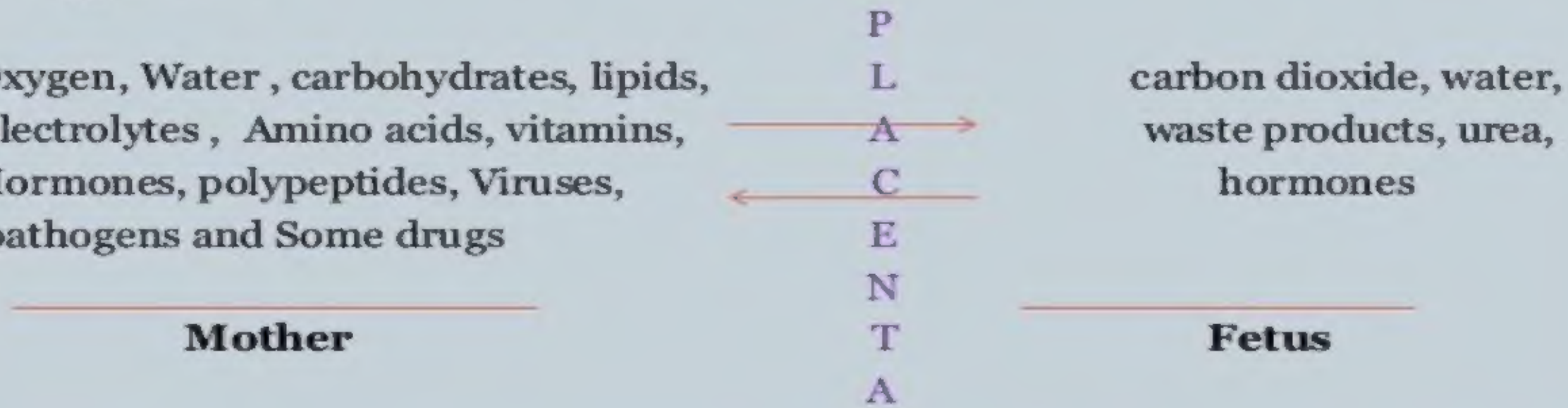
DRUG THERAPY DURING PREGNANCY AND LACTATION

PREGNANCY

INTRODUCTION

Pregnancy and drug use:

- 8% of pregnant women's need drug treatment and more than 90% pregnant women's take prescription or non-prescription drugs.
- 59% of pregnant women's are prescribed other than vitamin or mineral supplements and 13% of pregnant women's are prescribed with dietary supplements.



INTRODUCTON

Placental drug transfer:

The drug is transferred through placenta by passive diffusion and **the factors that affecting placental transfer are,**

- protein binding
- pH difference
- Molecular weight
- Lipid solubility

Physiological changes during pregnancy :

- Wt gain and altered body shape
- Frequent urination
- Mouth and tooth changes
- Aches and pains
- Nausea and vomiting (morning sickness)
- Heart burns and leg cramps

INTRODUCTION

Pharmacokinetic changes in pregnancy:

- Increase plasma volume (30-50%)
- Increase cardiac output
- Increase renal blood flow and GFR
- Increase body fat
- Increase hepatic metabolism
- Increase progesterone levels
- Decrease plasma albumin concentration

INTRODUCTION

Drugs to be used during pregnancy :

Condition	Drugs used
Nausea & vomiting	Cyclizine, Meclizine, Metoclopromide (safe in 3rd trimester of pregnancy)
Hypertension	Methyldopa
Cough	Diphenhydramine, Codeine, Dextromethorphan
Head ache	Paracetamol, codeine, Aspirin, Benzodiazepines & other NSAIDs (1st & 2nd trimester)
Anticoagulants	Heparin (S.C)
Anti- Amoebic drugs	Metoclopromide, Dilaxonide
Anti- migraine drugs	Ergometrine, Propranoloi, Amitryptelline
Allergic Rhinitis	Gluco-corticoids (locally), Diphenyl hydramine
Heart burns	Non-systemic antacids, Metoclopromide

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INTRODUCTION

Condition	Drugs used
Anti-diabetic drugs	Purified Insulin
Constipation	Milk of magnesia, Decussate sodium, Glycerin, Mineral oil, Bisacodyl
Peptic ulcer	Sucralfate, H2 blockers, non-systemic antacids, Bismuth sub- salicylates
Tuberculosis	Isoniazid, Ethambutol, Rifampin
Anti- asthmatics	Beta- agonists, Theophylline, Gluco-corticoids
Cardiac glycosides	Digoxin, Quinidine
Anti-malarial drugs	Cloroquine, Quinine
Anti-microbial drugs	Penicillin's, Cephalosporin's
Anti- helmintics	Piperazine, Biphenium

INTRODUCTION

ANTIBIOTICS CONTRAINDICATED DURING PREGNANCY :

DRUG	SIDE EFFECT
Metoclopromide	Hepatic failure
Chloramphenicol	Gray baby syndrome
Amino glycosides	Ototoxicity
Tetracycline's	Bone & teeth discoloration

TERATOGENESIS

TERATO – monster

GENESIS –producing

Teratogen is an infectious agent, drug, chemical/ radiant, that causes alterations in fetal morphology/ fetal functions when the fetus is exposed during critical stage of development.

Eg: 1. cleft lip/ palate, club foot, neural tube defects, missing/malformed limbs or fingers

2. Also behavioral and/ biochemical abnormalities

3. Teratogenesis is either direct i.e., malformation of structures or indirect, that interfering with Oxygen/ nutrients.

Malformation of drugs during pregnancy:

1. THALIDOMIDE:

This drug is 1st developed in Germany in 1954 by the pharmaceutical company i.e., chemie grunenthal.

- It is marketed in 1957 and spread to many countries like Europe, Asia, Australia, America& Africa.
- Thalidomide is used for insomnia, cold, cough, headache and morning sickness
- Used as anti- convulsive drug
- The 1st affected child birth are noticed in west Germany due to thalidomide on December 25, 1956. Later rare limb and ear defects are noticed & 40% of victims died before their 1st birthday.

because of this problems the thalidomide's are withdrawn from market by the end of November 1961.

Malformation of thalidomide:

phocomelia- it is derived from Greek word , in which

Phoco = seal

Melos = limbs

It indicates that the limb is like seal's flipper

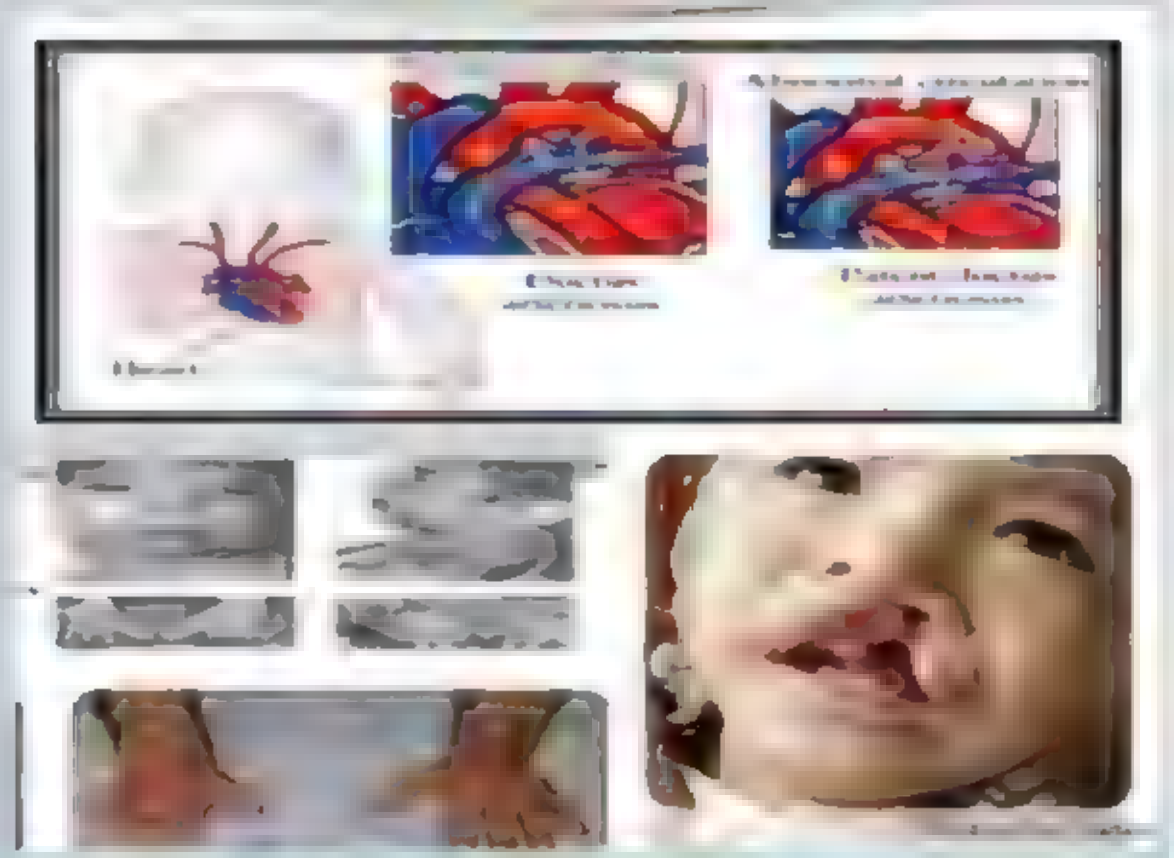
- No ear/ deafness
- Missing / extra fingers & toes
- Partial/ total sight
- Improper formation of heart, brain and other internal organs
- Flattening of bridge of nose

2. NSAIDs: if the NSAIDs are used 30 weeks on pregnancy onwards may causes,

- Premature closure of ductus arteriosus
- Oligohydramnios
- Deficiency of amniotic fluid

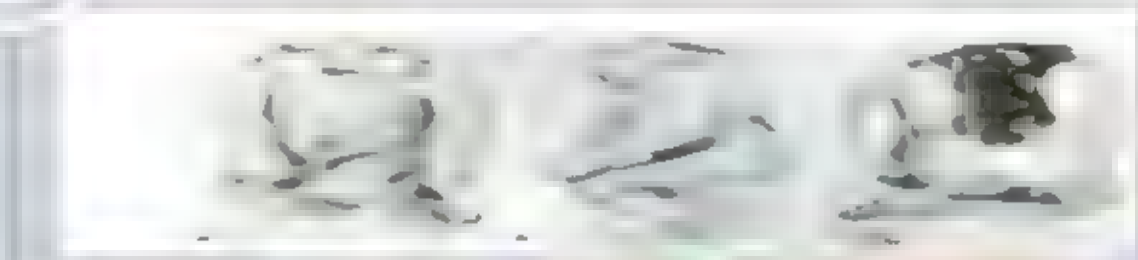
3. PHENYTOIN :

- Fetal hydantion syndrome
- Craniofacial abnormalities
- Hypo- plasia of distal phalanges
- Growth deficiency & mental deficiency
- Cleft Palate



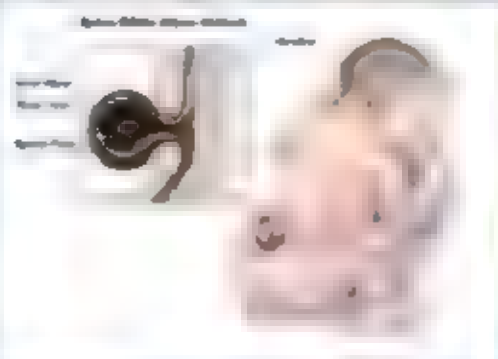
Implications

4. VALPROIC ACID: it decreases absorption of folic acid & may causes neural tube defects.



5. CARBAMAZEPINE :

- Craniofacial abnormalities
- Spinal bifida
- Hypo- plasia of distal phalanges



6. PHENOBARBITOL :

- Neonatal withdrawal
- Neonatal coagulopathy

7. SULPHONAMIDES:

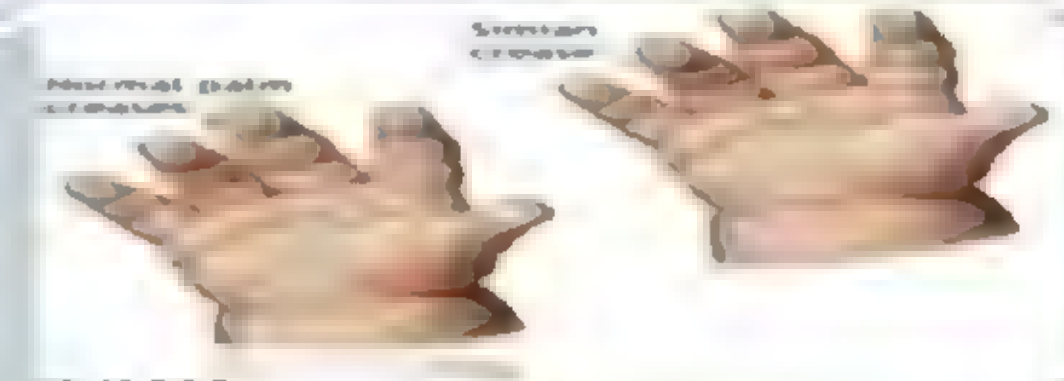
- Hyper bilirubinemia
- Jaundice
- Kernicterus

8. TRIMETHADIONE:

- Simian creases in the hands
- Cardiac anomalies
- Irregular teeth
- Mental retardation

9. DES (Diethyl stilbesterol):

- It increases risk of clear cell adeno-carcinoma of vagina & cervix
- Breast cancer have been found in daughters of women who took DES during pregnancy
- Fertility problems in daughters of pregnant women's



10. WARFARIN:

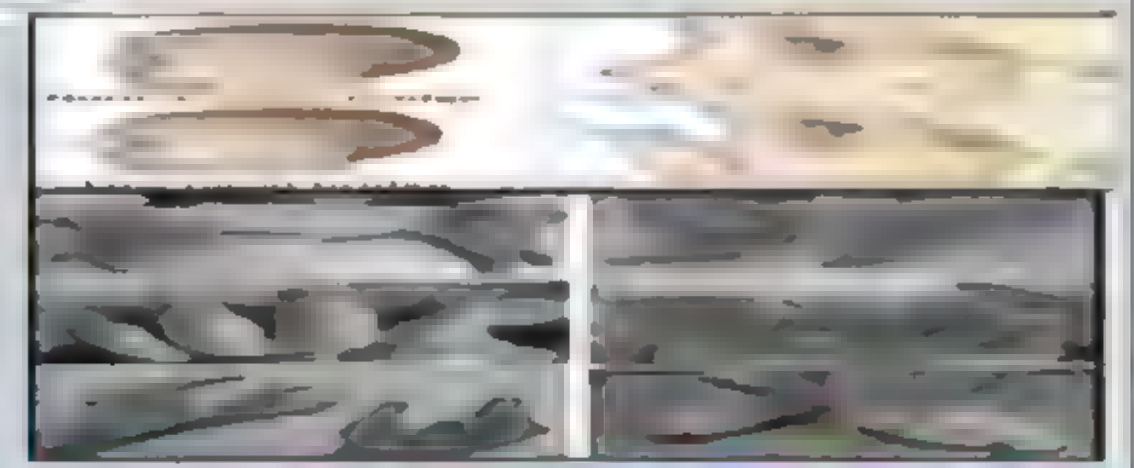
- Fetal warfarin syndrome
- Nasal hypo- plasia
- hypo- plasia of extremities
- Developmental retardation

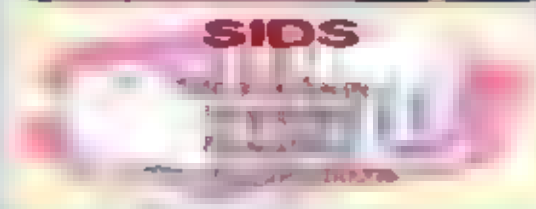
11. COCAINE AND OPIODS :

- Neonatal abstinence syndrome
- Inadequate growth of fetus
- Premature birth defects

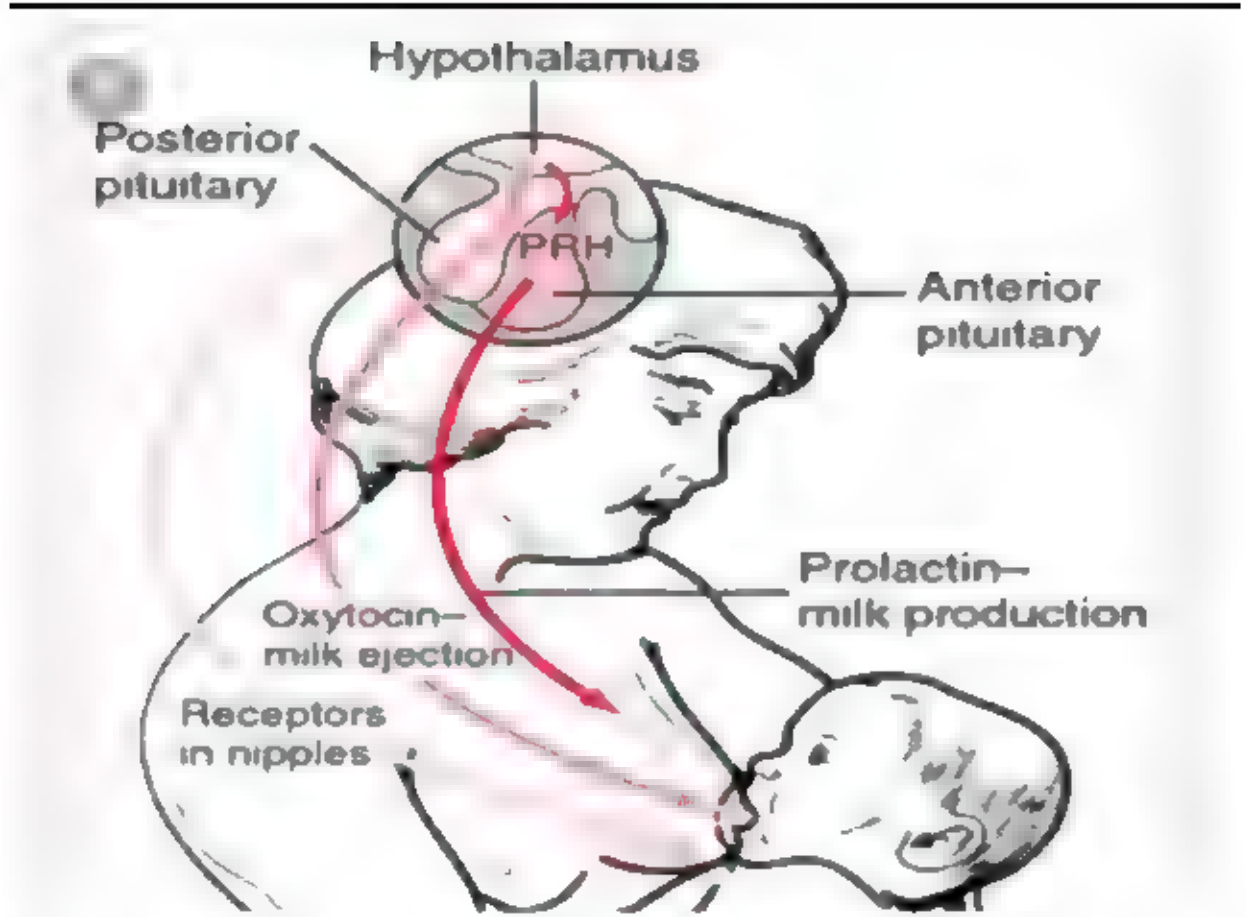
12. CIGARRATE SMOKING AND ALCOHOL CONSUMPTION :

- Birth defects in heart, brain and face
- Causes sudden infant death syndrome(SIDS)
- Premature labor and miscarriage
- Mental retardation





LACTATION


Hypothalamus
Posterior pituitary
PRH
Anterior pituitary
Prolactin–milk production
Oxytocin–milk ejection
Receptors in nipples

This is the best way to delivered nutrients into infants, through the mother's milk the nutrients are transferred into children's.

DRUG PASSAGE INTO BREAST MILK:

The drug is passed into milk either by diffusion or active transport.

- Diffusion – movement of drug from high to low concentration
- Active transport – movement of drug from low to high concentration
- After diffusion or active transport, the drug is passes into breast milk through spaces between alveolar cells.

DRUG TRANSFER INTO BREAST MILK:

- Ionization of drug – drugs which are non – protein bound non – ionized are more likely to be transferred into breast milk.
- Mol. Wt of drug – low mol. Wt drugs are more likely to be transferred into breast milk than high mol. Wt drugs.
- Solubility of drugs in lipids & water – lipid soluble drugs are easily soluble in breast milk than water soluble drugs.

DRUG CONCENTRATION IN BREAST MILK: The milk pH is lower than serum and variable in degree of fat concentration.

Changes in neonates:

- Vol. of milk consumed
- Higher gastric pH
- Difference in GI flora & GI transit time
- High concentration of drugs
- High % of body water
- Low metabolism & excretion rate

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INTRODUCTION

Safe drugs in nursing mothers :

Category	Example
Anti – microbial drugs	Penicillin's & Cephalosporin's
Analgesics	Paracetamol, Morphine, Pentazocine
Anti – hypertensive's	Beta – blockers, Ca2+ channel blockers
Anti – malarial drugs	Quinine, Chloroquine
Anti – tuberculotic's	Rifampin, Ethambutol, Pyrazinamide
Bronchodilators	Theophylline, Salbutamol
Anti – epileptic drugs	Phenobarbitone, Diphenyl hydantion, Valproic acid
Diuretics	Chlorthiazide, Furosemide, Spirano lactone
Hypoglycemic's	Insulin, Isoniazid, Tolbutamide

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Drugs to be avoided during lactation:

DRUG	EFFECT
Amiodarone	Neonatal hypothyroidism
Aspirin	Reye's syndrome
Barbiturate's	Drowsiness
Benzodiazepine's	Lathery
Coramphenicol	Gray baby syndrome
Carbimazole	Hypothyroidism
Contraceptives	Dimish milk supply, decreases N2 & protein content
Tetracycline's	Tooth discoloration
Ephedrine	Irritability

INTRODUCTION

- **Drugs which are contraindicated in nursing mother's:**
  Anti – cancer drugs, radio pharmaceuticals, ergot & it's derivatives, lithium, Thiouracil, Iodine, Mercurial's, sulphonamides, Atropine, chloramphenicol and phenyl butazone.
- **Drugs which suppress/inhibit Lactation:**
  Bromocriptine, Bendro - flumethiazide, Estradiol, Oral contraceptive's, Levodopa, Trazodone.
- **Drugs which are hazardous to Infants :**
  Large doses of Alcohol, Caffeine, Theophylline.

Considerations in breast feeding:

- With hole or delayed therapy if possible
- Use of drugs with poor penetration into milk
- Use an alternative route of administration
- Avoid nursing at peak concentration
- Pump & dump milk